

THE USEFULNESS OF PROSTATE SPECIFIC ANTIGEN SCREENING IN MALE PATIENTS PRESENTED WITH HAEMATURIA

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ABSTRACT

Background: In our study, we wanted to assess if prostate specific antigen (PSA) test is a useful test for patients presenting to our urgent clinics with Haematuria, or if it can be safely omitted, unless there were any clinical indication or after discussion with patients according to NICE guidelines.

Objective: Our objective is to review if the PSA test is a useful test that should be done routinely for all male patients presented to urgent clinic with haematuria in our practice in District hospital in UK.

Methods: We looked at retrospective data for 200 patients who presented with visible haematuria (VH) and non-visible haematuria (NVH) between 50-79 years old, between January 2016 and June 2017. All patients underwent digital rectal examination (DRE) and PSA testing as part of our standard investigation for haematuria.

Results: Out of 200 cases, 155 with visible haematuria, 10 of them underwent further investigations and two were diagnosed with prostate cancer and 45 with non-visible haematuria, 4 of them had further tests and none were diagnosed as prostate cancer. Overall number of patients who underwent further investigations is 14/200 (7%). Overall rate of prostate cancer diagnosis was 1%. The rate of diagnosis with visible haematuria 1.29%, and 0% with non-visible haematuria.

Conclusion: Despite using PSA as standard investigation for patients who are presented to urgent clinic with Haematuria, the rate of cancer diagnosis is very low (1%) and detected in patients with abnormal DRE, rather than elevated PSA. Our cancer detection rate 1% is less than those from ERSPC (8.2%), ProtecT (2.2%) and PLCO (1.4%). PSA should not be considered as a useful test of standard investigations for haematuria, unless abnormal DRE was found during examination.

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Keywords: Haematuria – PSA test – Prostate cancer.

Haematuria is a not an uncommon problem which keeps urologist across the country very busy. It is estimated that around 2.6% of the population may experience it during their lifetime¹. Haematuria could be the first presentation to all urological cancers especially bladder cancer and to a lesser extent advanced and invasive prostate

cancer, as well as to other benign conditions for example urinary tract infections, renal and ureteric stones. Haematuria is further classified into visible haematuria (VH) and non-visible haematuria (NVH). Non visible haematuria is defined as 3 or more red blood cells per high power field (HPF) in the absence of infection or proteinuria².

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PSA testing and screening has always been a controversial topic. There are three large randomised controlled trials (RCT) to assess the benefit of PSA screening; The European Randomised Study of Screening of Prostate cancer (ERSPC), The Prostate, Lung, Colorectal and Ovary cancer (PLCO), and ProtecT study.

The long running ERSPC study updated their 13 years of follow up results and concluded that 781 males need screening to detect 27 cases and to prevent one death³. The PLCO study showed a 4.9% overall rate of cancer detection⁴. PLCO also showed no evidence of mortality evidence compared to opportunistic screening at 13 years of follow-up⁵. Finally, the ProtecT study showed overall detection rate of 2.2%⁶. The overall conclusion from PLCO and ProtecT showed no difference in the disease specific mortality amongst the screened group compared to the control group. The ERSPC in 13 years follow up, revealed reduction in prostate cancer mortality due to PSA testing compared to their findings at 9 and 11 years. Despite these findings, the recommended further assessment of pros and cons of PSA testing prior to introduction of population based screening.

NICE guidelines recommend the consideration of PSA and digital rectal examination in patients with visible haematuria⁷. However, in view of the low detection rate and the low mortality rate in those three large RCTs, We retrospectively looked at our data to identify the usefulness of PSA testing in patients presenting with haematuria.

PATIENTS AND METHODS

We retrospectively examined data of 200 male patients aged 50-79 years presented to our urgent haematuria clinic with visible haematuria (VH) and non-visible haematuria (NVH) as their first presentation with no previous history of cancer between January 2016 and June 2017.

All patients were clinically assessed in a standardised manner with history and examination including digital rectal examination (DRE). They all underwent standard baseline investigations for haematuria, including urine dipstick, urine cytology, renal ultrasound scan, flexible cystoscopy, and blood tests including renal function tests and PSA. All patients had their PSA tested before DRE and flexible cystoscopy.

We followed the guidelines of the prostate cancer risk management programme (PCRMP) to identify elevated PSA⁸. That was updated in 2015 revealed the high variability of age specific values related to difference in demographics and clinical characteristics in a certain population⁹.

RESULTS

Out of the 200 cases included in our study 155 patients presented with VH and 45 presented with NVH.

Of those with VH, 134 patients had benign DRE and normal PSA test results. The remaining 21 cases had one or two parameters abnormal. For the purpose of interpretation they were further analysed in three groups.

The first group included 17 patients who had a benign DRE with an elevated age specific PSA. 11 patients had symptoms

suggesting urinary tract infection. They had a repeat PSA which came back within normal levels. Among the remaining 6 cases, two of them had chronically elevated PSA attributed to a large prostate gland. They continued to undergo Transurethral resection of prostate (TURP) which showed benign histology. The other 4 patients were investigated by MRI scan and only one of them proceeded to have Trans rectal ultrasound (TRUS) guided prostate Biopsy with negative malignancy results.

Table1: PSA Results

Age group	initial PSA		Repeat PSA	
	mean	median	mean	median
50 - 60	7.4	8	3.2	3.3
60 - 70	6.84	6.2	2.64	2.2
70 -80	9.6	8.9	4.9	5.3

The second group included only one patient who had an abnormal DRE and an elevated PSA 11.8 microgram/L, which is above the age specific range; he underwent further investigations in form of MRI scan, which showed T4 N1 disease. He

subsequently underwent TRUS guided prostate Biopsy to assess suitability for upfront chemotherapy and was confirmed to have a Gleason 8 prostate cancer.

The third group included three patients having abnormal DRE with normal age specific PSA, two of them underwent further investigations in form of TRUS guided prostate Biopsy and only one of them was diagnosed with Gleason 6 prostate cancer, the third case had MRI scan which suggested prostatitis, and no further action was taken of the 45 patients who presented with NVH all had a benign DRE and only 4 patients had an elevated PSA. Within those who had an elevated PSA Three were investigated by MRI scan and one of them had TRUS Biopsy with no malignancy found.

The overall number of patients who underwent further investigations was 14 of 200 total patients (7%). The overall rate of prostate cancer diagnosis was 1%. The rate of diagnosis with visible haematuria 1.29%, and 0% with non-visible haematuria.

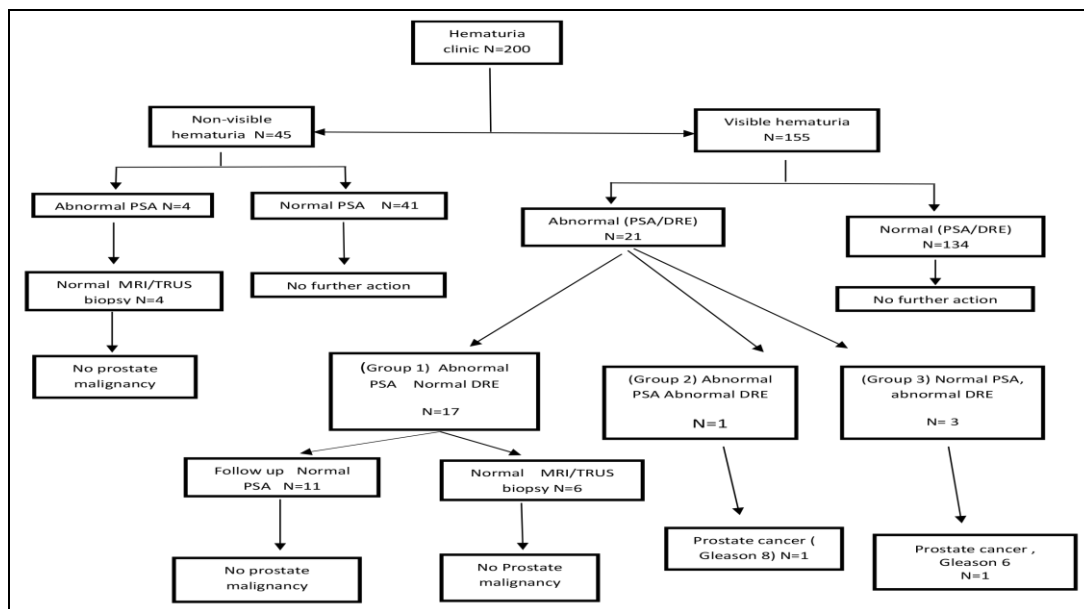


Figure 1: Flow-Chart of Findings.

DISCUSSION

Haematuria is one of the common urological presentations. The main causes of haematuria include urinary tract infection, urinary tract stones, trauma, renal parenchymal disease and urological cancers¹⁰. The common primary urological cancers presenting with haematuria are renal cell carcinoma, urothelial carcinoma and prostate cancer¹¹. Early cases of prostate cancer are not expected to present with haematuria as they usually arise in peripheral zone of the prostate away from the urethra, however locally advanced cases are expected to cause haematuria and are mostly detected by DRE¹².

In the work by Catalona et al 1994, where he compared the efficacy of DRE versus elevated PSA in early detection of prostate cancer. Elevated PSA detected more tumours (82%) than abnormal DRE (55%). When the two methods were combined, that increased the rate of detection of organ confined disease by 78% over DRE alone¹³. In our work, despite using PSA as a standard investigation for patients who presented to urgent clinic with haematuria, the rate of cancer diagnosis is very low (1%) and detected in patients with abnormal DRE, rather than elevated PSA.

Our prostate cancer detection rate of 1% is less than those from ERSPC, ProtecT and PLCO. There are similar studies in the literature looking at prostate cancer detection rate in patients with haematuria. Khadra et al in 2000 did a study on 1930 patients with haematuria, 1194 of them were men. Their prostate cancer detection rate was 0.7%¹⁴. Bromage et al in 2006 had an overall prostate cancer detection rate of 8% and 5.9% detection rate in men aged 50-79 in a study that contained 637

men. They recommended the use of PSA in clinical practice in the absence of prospective controlled trial at the time¹⁵. However, Chandrasekharan et al in 2009 did a similar study in men presenting with haematuria to their urgent clinic. They included 749 men with an overall prostate cancer detection rate of 3.7%. They recommended not to routinely use PSA in clinical practice unless patients are appropriately counselled¹⁶. The current NICE guidelines and European guidelines for PSA testing recommends consideration of the benefits and limitations of PSA testing before offering it to patients with suspected prostate cancer in the primary care^{17, 18}. The current European guidelines (EAU) also recommended individualised risk-adapted strategy for early detection to well-informed men with good performance status and 10 to 15 years life expectancy¹⁸. In conclusion, PSA testing should not be considered as a part of standard investigations for haematuria, unless an abnormal DRE was found during examination and after careful discussion of the benefits and limitations of PSA testing with the patient.

CONFLICT OF INTEREST

The above work has been accepted and presented as a poster presentation in 7th Emirates urological conference and 15th Arab urological conference–November 2018.

The abstract has been published subsequently in a supplement of the Arab journal of urology but not the main manuscript.

REFERENCES

1. King, K. and Steggall, M. Haematuria: from identification to treatment. *British Journal of Nursing*. 2014; 23 (Sup9), pp.S28-S32.
2. Rodgers M, Nixon J, Hempel S,Aho T, Kelly J, Neal D, et al. Diagnostic tests and algorithms used in the investigation of haematuria: systematic reviews and economic evaluation. *Health Technol Assess*. 2006;10(18):iii–iv. xi–259.
3. Schroder F.H.,Hugosson J, Roobol MJ, Tammela TL, Zappa M, Nelen V et al. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. *Lancet*. 2014; 384: 2027
4. Grubb RL 3rd, Pinsky PF, Greenlee RT,Izmirlian G, Miller AB, Hickey TP et al. Prostate cancer screening in the Prostate, Lung, Colorectal and Ovarian cancer screening trial: update on findings from the initial four rounds of screening in a randomized trial.*BJU Int*. 2008 Dec;102(11):1524-30.
5. Andriole GL, Crawford ED, Grubb RL 3rd, Buys SS, Chia D, Church TR,et al. Prostate Cancer Screening in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial:mortality results after 13 years of follow up. *J Natl Cancer Inst*. 2012 Jan, 18; 104(2)
6. Donovan J, Hamdy F, Neal D, Peters T, Oliver S, Brindle L, et al. Prostate testing for cancer and treatment (ProtecT) feasibility study. *Health Technol Assess* 2003;7(14):1—88.
7. Suspected Cancer: Recognition and Referral | Guidance and Guidelines | NICE." *Nice.org.uk*. N.p., 2018. Web. 14 Sept. 2018.
8. Prostate cancer risk management programme (PCRMP): benefits and risks of PSA testing.[online]. Available at: <https://www.gov.uk/government/publications/prostate-cancer-risk-management-programme-psa-test-benefits-and-risks/prostate-cancer-risk-management-programme-pcrmp-benefits-and-risks-of-psa-testing#fn:2> [Accessed 18 Sep. 2018]
9. Louie KS. UKNSC Screening for Prostate Cancer Review -2015 update. UK National Screening Committee, 2016.
10. O'Connor OJ, Fitzgerald E, Maher MM. Imaging of hematuria. *American Journal of Roentgenology*. 2010;195(4):W263–W267.
11. O'Connor OJ, McSweeney SE, Maher MM. Imaging of Hematuria. *Radiologic Clinics of North America*. 2008;46(1):113–132.
12. Roobol, M., Kranse, R., van der Crujisen, I. and Schröder, F. A more advanced clinical stage is positively correlated with an increased prostate cancer detection rate. *Urology*.2002; 59(1), pp.91-96.
13. Catalona, W., Richie, J., Ahmann, F., Hudson, M., Scardino, P., Flanigan, R., et al. Comparison of Digital Rectal Examination and Serum Prostate Specific Antigen in the Early Detection of Prostate Cancer: Results of a Multicenter Clinical Trial of 6,630 Men. *The Journal of Urology*.1994; 151(5), pp.1283-1290.

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14. Khadra M, Pickard R, Charlton M, Powell P, Neal D. A prospective analysis of 1,930 patients with hematuria to evaluate current diagnostic practice. *J Urol* 2000;163(2):524-7.
15. Bromage SJ, Napier-Hemy RD, Payne RD, Pearce I, McIntyre IG. The use of prostate-specific antigen testing in men presenting with haematuria. *BJU Int.* 2006 Dec;98(6):1221-4.
16. Chandrasekharan S, Shafik AA , and Eaton JD. PSA Testing of Men in the Haematuria Clinic, a Useful Additional Test or Unnecessary Investigation. *Journal of Clinical Urology.* 2010; Vol 3, Issue 1, pp. 11 - 14.
17. Prostate cancer risk management programme (PCRMP): benefits and risks of PSA testing. [online] Available at: <https://www.gov.uk/government/publications/prostate-cancer-risk-management-programme-psa-test-benefits-and-risks/prostate-cancer-risk-management-programme-pcrmp-benefits-and-risks-of-psa-testing>[Accessed 11 Dec.2019].
18. EAU Guidelines. Edn. presented at the EAU Annual Congress Copenhagen 2018. ISBN 978-94-92671-01-1.

پوخته

مفایئ پشکنینا دژکارا پروستاتا یا سنوردار لنگ وان نه خوشین توشی میزا خوینه لو بووین

نارمانجا: مه پیداجوونه که لدور رادیئ مفایئ تافیکرنا دژکارا پروستاتا جوړیه (PSA) لنگ نه خوشین رهگهز نیږ ټه وین سهرهدانا کلینیکا دهره کی یا بلهز لنگ مه کری ل نه خوشخانا دهقهرئ و توشی میزا خوینه لویئ بووین.

پیداجوون: ل داتایین 200 نه خوشان کر ب شیوازه کی شهگه کر گانندی ژ میزا خوینه لویا دیار (VH) دکهن یان میزا خوینه لو یا نه دیار دکهن، ته مهنئ وان دنافهرا 50 – 79 سالیئ بوو، دنافهرا 2016 و 2017 ههمی نه خوش کهنه بهر پشکنینا ریگه کی یا تبه کی (DRE) و تافیکرنا دژکارا پروستاتا جوړی (PSA) وهک پشکهک ژ پشکنینا پیقه ری یا میزا خوینه لو. ژ 200 حاله تان 155 حاله توشی میزا خوینه لویا دیار بووون، 10 ژ وان کهنه بهر پشکنینه کا زیده و دوو ب په نجه شیږا پروستاتا هاتنه دست نیشانکرن. ئ 45 حاله تین دی یین توشی میزا خوینه لو بووین 4 ژ وان کهنه بهر تافیکرنین زیده و چ وان ب په نجه شیږا پروستاتا نه هاتنه دست نیشانکرن.

سهرجه م: نه خوشین کهنه تینه بهر پشکنینین زیده گه هشته 200/14 (7 %) ، ئ تیکرایا گشتی یا دست نیشانکرنا په نجه شیږا پروستاتا 1 % بوو. تیکرایئ دست نیشانکرنی دگهل میزا خوینه لویا دیار 1,29 % و 0 % بوو دگهل میزا خوینه لویا نه دیار. ئ ل دو ماهیئ ههر چهنده دژکارا پروستاتا جوړی (PSA) هاته بکارئینان وهک پشکنینه کا پیقه ری بو وان نه خوشان ټه وین سهرهدانا کلینیکا بلهز یا میزا خوینه لو کری.

ئ دست نیشانکرنا په نجه شیږئ گه لهک یا کیم بوو (1 %) و ل نه خوشین پشکنینا ریگه یا تبه کی (DRE) یا نه سروشتی شوینا نه خوشیم دژکارا پروستاتا جوړی (PSA) یا بلند. تیکرایئ فه دیتنا په نجه شیږئ لنگ مه 1 % ټه وزی کیمتره ژ تیکرایئ خو ل ERSPC (2,8 %) و PLCO (4,1 %).

ټه فجا پیدفیه دژکارا پروستاتا جوړی (PSA) نه هیته هژمارتن وهک تافیکرنه کا مفادار بو پشکنینین پیقه ری یا میزا.

الخلاصة

فائدة فحص مستضد البروستاتا المحدد عند مرضى الذين يعانون من البول الدموي

الخلفية والأهداف: هدفنا هو مراجعة مدى فائدة اختبار مستضد البروستاتا النوعي (PSA) عند المرضى الذكور الذين راجعوا العيادة الخارجية العاجلة لدينا بمستشفى المقاطعة ويعانون من بيلة دموية.

طرق البحث: قمنا بمراجعة بيانات 200 مريض -بأثر رجعي- عانوا من بيلة دموية مرئية (VH)، أو بيلة دموية غير مرئية أعمارهم تتراوح بين 50-79 سنة، بين يناير 2016 ويونيو 2017.

خضع جميع المرضى لفحص المستقيم الأصبغي (DRE) واختبار مستضد البروستاتا النوعي (PSA) كجزء من الفحص المعياري للبيلة الدموية.

من بين 200 حالة، كان هناك 155 حالة مصابة ببيلة دموية مرئية خضع 10 منهم إلى مزيد من الفحوصات وتم تشخيص اثنين بسرطان البروستاتا، أما الـ 45 حالة الأخرى المصابون ببيلة دموية غير مرئية فقد خضع 4 منهم لمزيد من الاختبارات ولم يتم تشخيص أي منهم بسرطان البروستاتا.

العدد الإجمالي للمرضى الذين خضعوا لمزيد من الفحوصات هو 200/14 (7%)، أما المعدل العام لتشخيص سرطان البروستاتا فقد كان 1%. كان معدل التشخيص مع البيلة الدموية المرئية 1.29%، و0% مع البيلة الدموية غير المرئية.

في الختام، على الرغم من استخدام مستضد البروستاتا النوعي (PSA) كفحص معياري للمرضى بالذين راجعوا العيادة العاجلة ببيلة دموية، فإن معدل تشخيص السرطان منخفض جداً (1%)، ويكتشف في مرضى فحص المستقيم الأصبغي (DRE) غير الطبيعي بدلاً من مرضى مستضد البروستاتا النوعي (PSA) المرتفع.

النتائج: إن معدل اكتشاف السرطان لدينا 1% وهو أقل من معدله في (8.2%) ERSPC و (2.2%) ProtecT و (1.4%) PLCO.

وبناء عليه فلا ينبغي اعتبار مستضد البروستاتا النوعي (PSA) بمثابة اختبار مفيد للفحوصات المعيارية للبيلة الدموية في حال عدم وجود فحص مستقيم أصبغي (DRE) غير طبيعي.